Biophor Diagnostics, Inc.
Traditional Premarket Notification 510(k) Submission
RapidFRET Oral Fluid Assay for THC

510(k) Summary for the RapidFRET Oral Fluid Assay for THC

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92

The assigned 510(k) number is: K132096

Contact Information

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OCT 18 2013

Device Name, Common Name and Classification

RapidFRET Oral Fluid Assay for THC (Enzyme Immunoassay for Tetrahydrocannbinol)
RapidFRET Oral Fluid Calibrator Set (Clinical Toxicology Calibrator)
RapidFRET Oral Fluid Control Set (Drug Mixture Control Materials)

Product	Code	Class	Regulation Section	Panel
RapidFRET Oral Fluid Assay for THC	LDJ	II	862.3870	91 - Toxicology
RapidFRET Oral Fluid Calibrator Set	DKB	II	862.3200	91 - Toxicology
RapidFRET Oral Fluid Control Set	DIF	I	862.3280	91 - Toxicology

Identification of Legally Marketed Predicate Devices

Thermo Scientific CEDIA® Cannabinoids (THC) OFT Assay (k101744).

Device Description

The RapidFRET Oral Fluid Assay for THC is an In Vitro Diagnostic competitive immunoassay used to detect THC in human oral fluid. This is a ready-to-use homogenous system that involves energy transfer between an acceptor fluorophore labeled to an antibody and a donor fluorophore labeled to drug. The assay is based on competition between drug in the sample and drug labeled with the donor fluorophore for a fixed number of binding sites on the antibody reagent. When acceptor and donor fluorophores are brought into close proximity through a binding event, energy transfer occurs. The fluorescence resonance energy transfer (FRET) signal is measured at the wavelength of the acceptor fluorophore and is inversely proportional to the amount of drug in the sample. A Cutoff Calibrator is

used to translate the sample measurement into a positive or negative result. Controls are used to establish and monitor precision and accuracy.

Intended Use

The RapidFRET Oral Fluid Assay for THC is a homogeneous time-resolved fluorescence assay that is intended for prescription use in central laboratories only on the RapidFRET Integrated Workstation. The assay is used to perform a qualitative screen for Tetrahydrocannabinol at 4 ng/mL in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector. This assay provides only a preliminary result. To obtain a confirmed analytical result, a more specific alternate chemical method such as GC/MS or LC/MS/MS is required. Professional judgment should be applied to any drug test result, particularly when using preliminary positive results. For In Vitro Diagnostic Use Only.

The RapidFRET Oral Fluid THC Calibrator Set and RapidFRET Oral Fluid THC Control Set are intended for use only with theRapidFRET Oral Fluid Assay for THC and samples collected with the RapidEASE Oral Fluid Collector. The cutoff calibrator is used to determine the cutoff level and translate the assay measurement into a positive or negative result. The positive and negative controls are used to monitor laboratory systems, operators, precision, accuracy and assay conditions. For In Vitro Diagnostic Use Only.

Technological Similarities and Differences to the Predicate

	Candidate RapidFRET THC	**Predicate Thermo THC (k101744**
Indications for Use	Same	Qualitative determination of tetrahydrocannabinol (cannabinoid family) in human oral fluid.
Methodology	Same	Homogeneous competitive immunoassay.
Kit Components	1 THC specific antibody reagent in liquid, ready to use format. 1 THC drug conjugate reagent in liquid, ready to use format.	1 THC specific antibody reagent (marketed in combination as a lyophilized reagent and reconstitution buffer). 1 THC drug conjugate reagent (marketed in combination as a lyophilized reagent and reconstitution buffer).
Neat Oral Fluid Cutoff Level	4 ng/mL neat oral fluid.	3 ng/mL neat oral fluid.
Platform	RapidFRET Integrated Workstation	MGC240 analyzer
Sample Collection	Neat oral fluid is collected with the RapidEASE Oral Fluid	Oral fluid is collected with the Oral-Eze Saliva Collection

	Candidate RapidFRET THC	Predicate Thermo THC (k101744
	Collector via direct expectoration. No diluent is used and sample is stored in glass sample tube with inert screw cap.	System. This device uses an absorbent swab and diluent. Sample is stored in plastic tube with snap cap.
Principle and Procedure	Drugs in the oral fluid sample compete with the THC conjugate donor fluorophore for a fixed number of binding sites on the individual drug antibody acceptor reagents. When acceptor and donor fluorophores are brought into close proximity, through the binding event, fluorescent energy transfer is measured. The amount of drug in the specimen sample is inversely proportional to the assay signal as measured by time resolved fluorescence.	The assay is based on the sample analytes competing with analyte conjugates to one inactive fragment of β-galactosidase for antibody binding sites. The amount of drug in the specimen is inversely proportional to the assay signal as measured by absorbance.
Controls and Calibrator Levels	Calibrators are available at 0 ng/mL and 4 ng/mL. Controls are available at 2 ng/mL and 6 ng/mL.	Calibrators are available at 0 ng/mL, 1 ng/mL, and 10 ng/mL.

Brief Description of Study Data:

A series of studies were performed that evaluated the device performance characteristics including precision and analytical sensitivity, correlation with GC/MS and LC/MS/MS, cross reactivity, and analytical specificity that are summarized below.

Precision and Analytical Sensitivity

Three lots of the RapidFRET Oral Fluid Assay for THC were analyzed, four times daily, for a minimum of 20 days. Negative oral fluid pools were spiked with THC at 0%, 25%, 50%, 75%, 100%, 125%, 150%, 175% and 200% of the cutoff level corresponding to approximately 0, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0 and 8.0 ng/mL. The aggregate data is summarized in the table below:

THC	0%	25%	50%	75%	100%	125%	150%	175%	200%
POS	0	0	0	7	196	268	259	274	274
NEG	275	275	274	268	79	6	0	0	0
N	275	275	274	275	275	274	259	274	274

THC	0%	25%	50%	75%	100%	125%	150%	175%	200%
POS	0%	0%	0%	3%	71%	98%	100%	100%	100%
NEG	100%	100%	100%	97%	29%	2%	0%	0%	0%
N	275	275	274	275	275	274	259	274	274

The data indicate that the analytical sensitivity is between 75% and 125% of cutoff, and expected results were achieved at a >97% frequency.

Correlation with MS

Neat oral fluid was collected with the RapidEASE Oral Fluid Collection Device from volunteers potentially positive and negative for THC. The samples (n=236) were randomized and blinded to the instrument operator and assayed using RapidFRET THC reagents. Following screening, positive and negative samples were sent for confirmatory testing. The summarized data are shown below.

n = 236	MS POS	MS NEG
RapidFRET POS	91	2[†]
RapidFRET NEG	2[§]	141
% Agreement	98%	99%

[†]Samples contained 3.4 and 3.7 ng/mL THC. [§]Samples contained 4.5 and 4.6 ng/mL THC.

The data indicate that the RapidFRET Oral Fluid Assay for THC was accurate >98% of the time in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector.

Cross Reactivity and Analytical Specificity

A compound library of 167 different structurally related and unrelated compounds including metabolites, OTC and prescription medications and drugs of abuse was used to evaluate the device cross reactivity and specificity. Compounds were spiked at 30,000 ng/mL into neat oral fluid pool aliquots with 0 ng/mL, 2 ng/mL and 6 ng/mL THC, processed with the RapidEASE Collector, and tested with the RapidFRET THC assay. Those compounds that gave an unexpected result were further titrated to determine the concentration at which the cross-reacting compound yielded a result approximately equivalent to the cutoff. Six structurally related compounds were determined to cross-react below 10,000 ng/mL in the absence of THC.

Compound	Level (ng/mL)	0% THC† (0 ng/mL)	50% THC† (2 ng/mL)	150% THC† (6 ng/mL)
Structurally Related Compounds That Cross React in Neat Oral Fluid Pool with 0 ng/mL THC				
11-Hydroxy-d9-THC	30,000	10 [40%]	POS	POS
Cannabidiol	30,000	6,400 [0.6%]	POS	POS
Cannabinol	30,000	8 [50%]	POS	POS
d8-THC	30,000	46 [8.7%]	POS	POS
d8-THC Acid	30,000	4 [100%]	POS	POS

Compound	Level (ng/mL)	0% THC† (0 ng/mL)	50% THC† (2 ng/mL)	150% THC† (6 ng/mL)
Structurally Related Compounds That Cross React in Neat Oral Fluid Pool with 0 ng/mL THC				
d9-THC Acid	30,000	6 [67%]	POS	POS

†Results are presented as either the RapidFRET THC screening result (POS / NEG) or the concentration in ng/mL of the cross-reactant that gives a Cutoff equivalent response. Values in square brackets represent percent cross reactivity.

A second study evaluated common substances such as foods and dental products as well as pH variations. HSA, ethanol, baking soda, whole blood, hemoglobin, hydrogen peroxide, sodium chloride, cholesterol, denture adhesive, ascorbic acid, bilirubin, IgA, IgG and IgM were spiked into neat oral fluid pool aliquots that contained either 2 ng/mL or 6 ng/mL of THC. Neat oral fluid pool was titrated to pH values of 5, 6, 7, 8 and 9, spiked with THC to 2 ng/mL or 6 ng/mL and assayed with the RapidFRET THC Assay. The effects of antiseptic mouthwash, cough syrup, cranberry juice, orange juice, tooth paste, chewing tobacco, cigarettes, chewing gum, hard candy, teeth whitening strips, cola, water, antacid, coffee and tea were evaluated by asking volunteers to use a specific item and provide an oral fluid sample. These samples were then spiked with THC to 2 ng/mL or 6 ng/mL, processed with a RapidEASE Collector and assayed with the RapidFRET THC assay. All compounds at the listed concentrations gave a NEG result when spiked with 2 ng/mL THC and a POS result when spike with 6 ng/mL THC.

Conclusions

The RapidFRET Oral Fluid Assay for THC including the RapidFRET Oral Fluid Negative and Cutoff Calibrators, the RapidFRET Oral Fluid Negative and Positive Controls and the RapidEASE Oral Fluid Collector were determined to be safe and effective for their intended use.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

October 18, 2013

BIOPHOR DIAGNOSTICS, INC.
c/o Nathaniel Butlin, Ph.D.
1201 Douglas Ave
REDWOOD CITY CA 94063

Re: K132096
Trade/Device Name: RapidFRET Oral Fluid Assay for THC
RapidFRET Oral Fluid Calibrator Set
RapidFRET Oral Fluid Control Set
Regulation Number: 21 CFR 862.3870
Regulation Name: Cannabinoid test system
Regulatory Class: II
Product Code: LDJ, DKB, DIF
Dated: September 10, 2013
Received: September 27, 2013

Dear Dr. Butlin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carol E. Benson -S for

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*

k132096

Device Name

RapidFRET Oral Fluid Assay for THC, RapidFRET Oral Fluid Calibrator Set, RapidFRET Oral Fluid Control Set, RapidEASE Oral Fluid Collector

Indications for Use *(Describe)*

The RapidFRET Oral Fluid Assay for THC is a homogeneous time-resolved fluorescence assay that is intended for prescription use in central laboratories only on the RapidFret Integrated Workstation. The assay is used to perform a qualitative screen for Tetrahydrocannabinol at 4 ng/mL in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector. This assay provides only a preliminary result. To obtain a confirmed analytical result, a more specific alternate chemical method such as GC/MS or LC/MS/MS is required. Professional judgment should be applied to any drug test result, particularly when using preliminary positive results. For In Vitro Diagnostic Use Only.

The RapidFRET Oral Fluid THC Calibrator Set and RapidFRET Oral Fluid THC Control Set are intended for use only with theRapidFRET Oral Fluid Assay for THC and samples collected with the RapidEASE Oral Fluid Collector. The cutoff calibrator is used to determine the cutoff level and translate the assay measurement into a positive or negative result. The positive and negative controls are used to monitor laboratory systems, operators, precision, accuracy and assay conditions. For In Vitro Diagnostic Use Only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Denise Johnson-Iyles -S